

Message Text

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PAGE 01 STATE 073508
ORIGIN HEW-06

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FM SECSTATE WASHDC

TO AMEMBASSY CANBERRA PRIORITY

UNCLAS STATE 073508

E.O. 11652: N/A

TAGS: TBIO, AS

SUBJECT: WITHDRAWL FROM SALE OF DRUG PHENFORMAN
PASS AUSTRALIAN DEPARTMENT OF HEALTH
REF: CANBERRA 2037

1. PHENFORMIN (DB1, MELTROL), A BIGUANIDE DERIVATIVE, IS AN ORAL HYPOGLYCEMIC AGENT THAT IS COMPLETELY UNRELATED TO THE SULFONYLUREAS (TOLBUTAMIDE-ORINASE, CHLORPROPAMIDE-DIABINESE, TOLZAMIDE-TOLINASE, ACETOHEXAMIDE-DYMELOR) IN CHEMICAL STRUCTURE AND IN MODE OF ACTION. ITS SPECIFIC MECHANISM OF ACTION IS UNKOWN. UNLIKE THE SULFONYLUREAS, IT EXERTS ITS HYPOGLYCEMIC EFFECT THROUGH AN EXTRAPANCREATIC MECHANISM AND DOESN'T STIMULATE INSULIN PRODUCTION. IT IS BELIEVED TO DECREASE GLUCONEOGENESIS, INHIBIT THE INTESTINAL ABSORPTION OF GLUCOSE, AND IN VITRO HAS BEEN SHOWN TO INCREASE GLUCOSE UTILIZATION BY ENHANCING ANAEROBIC GLYCOLYSIS. THIS LAST-NAMED ACTION IS THOUGHT TO OCCUR AS A RESULT OF, OR COINCIDENT WITH, AN INHIBITION OF CELLULAR
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RESPIRATION AND AS A CONSEQUENCE THE CONCENTRATION OF LACTATE INCREASES.

2. THERE HAVE BEEN NUMEROUS REPORTS OF LACTIC ACIDOSIS AN OFTEN FATAL METABOLIC ACIDOSIS, IN PATIENTS RECEIVING PHENFORMIN. (AT LEAST 552 CASES HAVE BEEN REPORTED DURING THE LAST 13 YEARS) THUS THE FDA'S ENDOCRINOLOGY AND

METABOLISM ADVISORY COMMITTEE HAS BEEN STUDYING THE IMPLICATION OF THIS ADVERSE REACTION. RECENTLY THEY RECOMMENDED THE REMOVAL OF PHENFORMIN FROM THE MARKET AFTER HEARING PRESENTATIONS FROM FDA CONSULTANTS AND A GROUP OF EXPERTS FROM CIBA-GEIGY. THIS ACTION IS BASED ON THE BELIEF THAT A CASUAL RELATIONSHIP HAS BEEN ESTABLISHED BETWEEN THE USE OF THE DRUG AND LACTIC ACIDOSIS.

3. CIBA-GEIGY ON THE OTHER HAND STATES THAT LACTIC ACIDOSIS IS A KNOWN, THOUGH UNCOMMON, COMPLICATION OF DIABETES. THERE ARE MANY CAUSATIVE FACTORS OF LACTIC ACIDOSIS, AND IN SUSCEPTIBLE PATIENTS, PHENFORMIN APPEARS TO BE ONE OF THEM. MOREOVER, LACTIC ACIDOSIS ALSO HAS BEEN SEEN IN PATIENTS RECEIVING OTHER ORAL ANTIDIABETIC AGENTS AND INSULIN. FURTHERMORE, THEY INSISTED THAT PHENFORMIN SHOULD NOT BE USED IN CLINICAL SITUATIONS THAT PREDISPOSE TO LACTIC ACIDOSIS; SUCH AS, EXCESSIVE USE OF ALCOHOL, CERTAIN CARDIAC DISEASES, KIDNEY DISEASE OR LIVER DISEASE.

4. IN CONCLUSION, PHENFORMIN CONTINUES TO BE MARKETING, BUT THE FDA'S ENDOCRINOLOGY AND METABOLISM ADVISORY COMMITTEE RECOMMENDS ITS REMOVAL FROM THE MARKET. AT THIS TIME, THE FUTURE MARKETING STATUS OF THIS DRUG IS UNCERTAIN.

5. SUMMARY OF TRANSCRIPT OF 15TH MEETING FDA ENDOCRINOLOGY AND METABOLISM ADVISORY COMMITTEE BEING AIRMAILED TO EMBASSY TO PASS TO AUSTRALIAN DEPARTMENT OF HEALTH.
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Decaption Date: 01-Jan-1960 12:00:00 am
Decaption Note:
Disposition Action: n/a
Disposition Approved on Date:
Disposition Case Number: n/a
Disposition Comment:
Disposition Date: 01-Jan-1960 12:00:00 am
Disposition Event:
Disposition History: n/a
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